

CEPH-0418

**WHAT IS CLAIMED IS:**

1. An isolated receptor which binds glial cell lined-derived neurotrophic factor (GDNF), said receptor comprising at least one polypeptide having a molecular weight selected from the group consisting of polypeptides of about 55 kD, 70kD, 135kD, and 300kD molecular weight, as determined by SDS-PAGE on 4-20% gradient gels.
2. A competitive assay for identifying compounds which bind to GDNF receptors comprising
  - a) incubating said compounds with cells which express c-RET receptors in the presence of an excess of labeled GDNF;
  - b) measuring the amount of labeled GDNF bound to said cells; and
  - c) comparing amount labeled GDNF bound to said cells to that of controls not incubated with said compounds.
3. The method of claim 2 wherein the cells are selected from the group consisting of NB2/a, MN-1, and PC12 cells.
4. The method of claim 2 wherein the labeled GDNF is <sup>125</sup>I-GDNF.
5. A competitive assay for identifying compounds which bind to isolated GDNF receptors comprising
  - a) incubating said compounds with isolated c-RET receptors in the presence of an excess of labeled GDNF;
  - b) measuring the amount of labeled GDNF bound to said receptors; and
  - c) comparing amount labeled GDNF bound to said receptors to that of controls not incubated with said compounds.

6. The method of claim 5 wherein the receptors are polypeptides which bind GDNF selected from the group consisting of polypeptides about 55kD, 70kD, 135kD, 155kD, and 300kD molecular weight.

7. The method of claim 6 wherein the polypeptide is about 155kD molecular weight.

8. The method of claim 5 wherein the isolated receptor is c-RET.

9. The method of claim 5 wherein the labeled GDNF is <sup>125</sup>I-GDNF.

10. A method for identifying compounds which are GDNF homologs comprising  
a) incubating said compounds with cells which express c-RET receptors; and  
b) determining whether said compound effects tyrosine phosphorylation.

11. The method of claim 10 wherein said cells are selected from the group consisting of PC12, MN-1, and NB2/a.

12. A method for identifying compounds which are GDNF homologs comprising  
a) incubating said compounds with cells which express c-RET receptors; and  
b) determining whether said compounds effect an increase in *c-fos* mRNA levels.

13. The method of claim 12 wherein said cells are selected from the group consisting of PC12, MN-1, and NB2/a.

14. A method for identifying compounds which are GDNF homologs comprising  
a) incubating said compounds with cells which express c-RET receptors under non-permissive conditions for said cells; and  
b) determining the number of surviving cells as compared to controls not incubated with said compounds.

15. The method of claim 14 wherein said cells are selected from the group consisting of PC12, MN-1, and NB2/a.

16. A method for identifying compounds which are GDNF analogs comprising  
a) incubating said compounds with cells which express c-RET receptors in the presence of concentrations of GDNF effective for phosphorylating tyrosine; and  
b) determining whether said compounds effect a decrease in the tyrosine phosphorylation as compared with controls not incubated with said compounds.

17. The method of claim 16 wherein said cells are selected from the group consisting of PC12, MN-1, and NB2/a.

18. A method for identifying compounds which are GDNF analogs comprising  
a) incubating said compounds with cells which express c-RET receptors in the presence of concentrations of GDNF effective for increasing *c-fos* mRNA levels; and  
b) determining whether said compounds effect a decrease in *c-fos* mRNA levels as compared with controls not incubated with said compounds.

19. The method of claim 18 wherein said cells are selected from the group consisting of PC12, MN-1, and NB2/a.

20. A method for identifying compounds which are GDNF analogs comprising  
a) incubating said compounds with cells which express c-RET receptors under non-permissive conditions for said cells in the presence of amount of GDNF effective for cell survival; and  
b) determining the number of surviving cells as compared with controls not incubated with said compounds.

21. The method of claim 20 wherein said cells are selected from the group consisting of PC12, MN-1, and NB2/a.

- 22. Isolated GDNFR- $\beta$  comprising the amino acid sequence of SEQ ID NO:2.
- 23. Isolated GDNFR- $\beta$  comprising the amino acid sequence of SEQ ID NO:9.
- 24. A compound comprising the amino acid sequence of SEQ ID NO:2.
- 25. A compound comprising the amino acid sequence of SEQ ID NO:9.
- 26. An isolated nucleic acid having the sequence of SEQ ID No:5.
- 27. An isolated nucleic acid having the sequence of SEQ ID No: 10.